No evidence that vaccines cause insulin dependent diabetes mellitus

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Histological and serological findings in insulin dependent diabetes mellitus (IDDM) are consistent with autoimmune causes and recent work suggests polygenic inheritance. The incidence in developed countries seems to be increasing,[1] although it is unclear whether this finding is real or artefactual. Given the age of the victims of IDDM and marked differences in incidence of the disease in children under 15[1] (see table 1), international attention has began focusing on the nature of possible external stimuli in the genesis of IDDM. Among these, vaccination schedules have been also called into question as possible modulating factors. Classen and Classen have postulated a protective effect of exposure to immunogens if babies are vaccinated within 42 days from birth.[2] It is known that genetic manipulation in animal models followed by early challenge with vaccine antigen can precipitate onset of

Table 1 Incidence of insulin dependent diabetes mellitus in children under 15 years of age from registers of selected worldwide countries. Incidence estimates are derived from national or subnational registers. After Karvonen et al[1]

Region *Country*	*Study period*	*Incidence rates per 100 000*
Africa		
Algeria	1980–89	8.1
Tanzania	1982–91	0.8
Sudan	1987–90	6.4
North America		
Canada	1971–85	9.8
Cuba	1978–80	2.7
Mexico	1984–86	0.6
Puerto Rico	1985–89	10.0
United States		
North Dakota	1980–86	18.9
Wisconsin	1970–79	18.2
Allegheny County	1970–85	17.3
Rochester	1965–79	17.1
Colorado	1978–88	15.5
San Diego	1978–81	9.4
South America		
Brazil	1987–91	7.6
Chile	1990–91	2.5
Asia		
Israel	1975–80	4.5
Japan	1974–86	1.7
Kuwait	1980–81	4.0
Republic of Korea	1985–86	0.6
Russia	1983–89	4.6
Oceania		
Australia	1985–89	13.2
Europe		
Denmark	1989–90	21.5
Finland	1987–89	35.3
France	1989–90	7.8
Germany	1960–89	7.4
Greece	1989–90	9.3
Italy	1989–90	6.8
Latvia	1983–88	6.5
Malta	1980–87	13.6
Netherlands	1989–90	11.0
Norway	1989–90	20.8
Poland	1989–90	5.5
Portugal	1989–90	7.5
Romania	1989–90	5.1
Slovenia	1988–90	6.5
Spain	1985–88	10.9
Sweden	1978–87	24.4
United Kingdom	1988	13.5

Table 2 Template grid used to select studies by topic

IDDM
Other autoimmune disease
- Occurence of disease
- Natural history
- Risk factors
  - vaccination
  - infections
  - genetic factors
  - socioeconomic factors
  - environmental factors
  - other
- Autoimmunity
- Mechanisms of immunity
- T cell vaccination

Table 3 Checklist used to assess study relevance and quality

1. Review : Immunisation and IDDM
2. Study identity
   - 2.1 Study number:
   - 2.2 First author:
   - 2.3 Country:
   - 2.4 Institution:
   - 2.5 Sponsorship:
   - 2.6 Vancouver (Journal. Year; volume: pages)
3. Issues covered by the study
   - IDDM
   - Other autoimmune disease
   - Occurrence of disease
   - Natural history
   - Risk factors
     - vaccination
     - infections
     - genetic factors
     - socioeconomic factors
     - environmental factors
     - other
   - Autoimmunity
   - Mechanisms of immunity
   - T cell vaccination
4. Study design
   - 4.1 Type of study
     - descriptive
     - case study
     - analytical prospective
     - analytical retrospective
     - migrant study
     - experimental
     - review
     - comment
     - editorial
     - other

   (only for experimental and analytical studies)
   - 4.2 Comparisons:
   - 4.3 Outcome measures:
   - 4.4 Follow up duration (for each outcome measure)
5. Study population (only for experimental and analytical studies)
   - 5.1 Human or animals:
   - 5.2 Human population (general, at risk):
   - 5.3 At risk group(s):
6. Quality of the study (only for experimental and analytical)
   - 6.1 Internal validity
   - 6.1.1 selection bias (self selection, diagnostic bias, etc)
   - 6.1.2 information bias (misclassification, recall bias)
   - 6.1.3 Confounding
   - 6.2 External validity (inference from study to target population)
   - 6.3 Precision (study size, etc)
7. Soundness of the methods
   - 7.1 Internal coherence (from aim to conclusions)
   - 7.2 Detailed reporting
   - 7.3 Appropriateness of statistical methods
8. Study results

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IDDM.[3] We report the results of a study aimed at assembling, examining, and summing up evidence of the possible link between vaccination schedules in humans and onset of IDDM. We carried out an exploratory review of current state of knowledge of human autoimmune disease, the causation of IDDM, and its possible links to human vaccination. By means of extensive searches of Medline, Embase, Biosis Previews, Current Biotechnology Abstracts, and Derwent Biotechnology Abstracts databases using ad hoc strategies we identified 95 possible studies. Selection was based on their coverage of at least one of the issues in the template grid in table 2. We assessed the quality and content of each selected paper using the checklist at table 3.

Of the 95 studies, we assessed 54 as possibly relevant of which only six directly tackled the study question. We interviewed eight researchers active in investigating trigger factors for IDDM. Evidence of a causal link in humans was sought by reviewing a sample of 12 large trials and two meta-analyses of paediatric vaccines.

We found that international analytical literature is insufficient and of limited coverage to shed light on the possible link between onset of IDDM and vaccination. There seem to be no reviews of the subject and no evidence in humans. The papers that explored the relation between vaccination and IDDM either did not find evidence of the causal link or found evidence against such a link. A Swedish childhood diabetes study found a significant decrease in odds ratio for measles vaccination (OR = 0.69; CI: 0.48, 0.98) and no significant effect for tuberculosis, smallpox, tetanus, whooping cough, rubella and mumps vaccines.[4] According to Hyoty[5] the elimination of natural mumps by the MMR vaccination may have decreased the risk of developing IDDM in Finland and a recent epidemiological study found no difference in cumulative incidence rates of IDDM between two cohorts of children born before and after the exclusion of pertussis vaccine from the national vaccination schedule.[6] The available experimental evidence does not allow any assessment of the links between time of vaccination and onset of IDDM as the 12 large randomised controlled trials and the two meta-analyses that we examined were not designed to capture long term possible adverse events such as IDDM. We conclude that at present there is no evidence of a link between IDDM and vaccination in humans.

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Readers interested in the full details of methods used in the review should contact Professor Jefferson.

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